

Digestive Diseases

NEWS

National Digestive Diseases Information Clearinghouse

Winter 2008

NIH Roadmap Initiative Focuses on Microorganisms

A major research project involving the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and other components of the National Institutes of Health (NIH) will help scientists understand the role bacteria, fungi, and other microbes play in human health and disease. The Human Microbiome Project (HMP) will help develop research tools and strategies to improve understanding, treatment, and prevention of inflammatory bowel disease, obesity, diabetes, and other health conditions.

“The Human Microbiome Project will help us understand the microbial environment in the gut, as well as provide us with the tools and technology to expand our exploration into this field of research,” said NIDDK Director Griffin P. Rodgers, M.D., M.A.C.P., co-chair of the HMP’s Implementation Group.

The estimated 10 to 100 trillion microorganisms that inhabit the human body actually outnumber the body’s own cells by a factor of 10. The human microbiome is the genetic sum of this community of microorganisms. Scientists are finding some surprising ways human-associated microbes influence human health and vice versa.

For example, NIDDK-funded research led by Jeffrey Gordon, M.D., at Washington University in St. Louis, suggests gut bacteria may affect body weight. Gordon’s group correlated weight loss in obese individuals with a change in the relative abundance of the two major types of gut bacteria—*Firmicutes* and *Bacteroidetes*. As study

participants lost weight on either of two types of low-calorie diets, the proportional representation of the *Bacteroidetes* increased significantly. In studies using mice, Gordon’s group has shown that gut bacteria not only affect the body’s ability to extract calories from food but also regulate host genes involved in energy metabolism.



Major Scientific Resource

The HMP, with \$115 million in funding for 5 years, officially became an NIH Roadmap for Medical Research initiative last May. Roadmap initiatives address major opportunities or gaps in research that no single institute can tackle alone.

HMP,

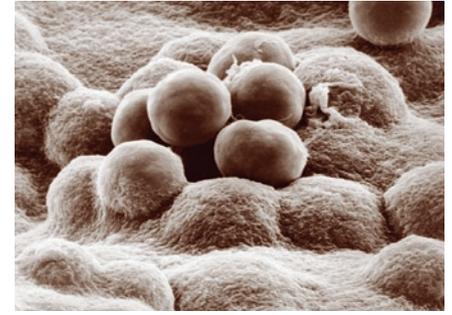
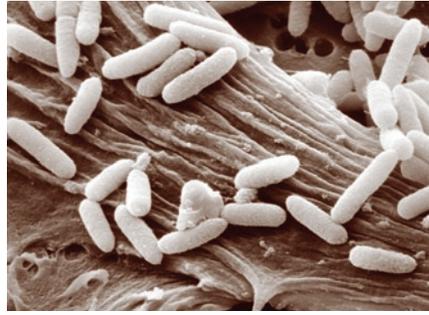
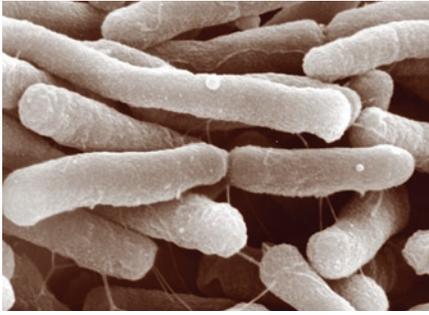
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NIDDK
NATIONAL INSTITUTE OF
DIABETES AND DIGESTIVE
AND KIDNEY DISEASES



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From left, scanning electron micrographs of the human-associated bacteria *Escherichia coli*, *Pseudomonas aeruginosa*, and *Neisseria meningitidis*. Photo credit: Thomas Moninger, University of Iowa Central Microscopy Research Facility.

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The HMP's first goal is to assemble a reference database containing the genomes of human-associated microorganisms. The HMP has already begun sequencing the genomes of human-associated microbes that are cultivable. Later on, the project will focus on strategies to cultivate and sequence organisms that do not grow in a lab. With the help of various partners, the HMP plans to sequence the genomes of about 1,000 different organisms.

"The Human Microbiome Project is essentially an enormous survey of the bacteria that populate our gut and other sites and what they are doing there," said Robert Karp, Ph.D., the NIDDK's director of the Genetics and Genomics Programs, Division of Digestive Diseases and Nutrition, and representative for the NIH Human Microbiome Working Group. "It is going to be a major scientific resource for researchers."

The Human Microbiome Project (HMP) will help develop research tools and strategies to improve understanding, treatment, and prevention of inflammatory bowel disease, obesity, diabetes, and other health conditions.

Like the Human Genome Project, which deciphered the human DNA code, data from the HMP will be a public resource available not only to NIH researchers but to scientists around the globe.

Microbial Diversity

The project will also begin to examine the diversity of the human microbiome by sampling a number of specific body sites including the gut, vagina, mouth, nose, and skin of volunteers. This process will help scientists gauge the breadth of the human microbiome and begin to answer the following questions:

- Do humans have a core microbiome, or a set of microbes that is fundamentally different from other host species?
- What factors, such as diet and the use of antibiotics, influence the microbiome?

HMP,

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Digestive Diseases NEWS

Digestive Diseases News, an email newsletter, is sent to subscribers by the National Digestive Diseases Information Clearinghouse (NDDIC). The newsletter features news about digestive diseases, special events, patient and professional meetings, and new publications available from the NDDIC and other organizations.

If you would like to subscribe, go to <http://catalog.niddk.nih.gov/newsletter.cfm>. You can read or download a PDF version of the newsletter at <http://digestive.niddk.nih.gov/about/newsletter.htm>.



Executive Editor: Stephen P. James, M.D.

Stephen P. James, M.D., is the director of the Division of Digestive Diseases and Nutrition within the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). As director, Dr. James oversees planning, implementation, and evaluation of a national research effort focused on gastrointestinal, pancreatic, hepatobiliary, and nutrition diseases and conditions. Before joining the NIDDK in 2001, Dr. James directed the division of gastroenterology at the University of Maryland's School of Medicine for 10 years.



Hopefully, new technologies will emerge from the project that will allow scientists to study microorganisms within the context of the human microenvironment and complex human microbe interactions.

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- Does the microbiome change with age?
- How does the microbiome correlate with health and disease?

“This is a pilot project,” said Jane Peterson, Ph.D., HMP program director and associate director of extramural research at the NIH National Human Genome Research Institute. According to Peterson, the HMP will not define the microbiome for all people and health conditions but will establish the resources and demonstrate strategies researchers need to conduct disease-specific research.

New Research Tools

Hopefully, new technologies will emerge from the project that will allow scientists to study microorganisms within the context of the human microenvironment and complex human microbe interactions. The HMP also will develop new computational analysis tools to make sense of the very complex data the project will generate.

In December 2007, HMP working group members met with scientists outside the United States to discuss the creation of an international consortium to coordinate efforts to characterize the human microbiome. For more information about the HMP and the NIH Roadmap project, go to www.nihroadmap.nih.gov. ■

Probiotics: Friendly Bacteria

Probiotics—sold as supplements in capsule form and as ingredients in foods such as yogurt, cheese, baby food, and energy bars—are live microorganisms that people consume for anticipated health benefits. Prebiotics are foods or ingestible substances that stimulate the growth or activity of probiotics.



The idea of ingesting microorganisms for the sake of health has been around at least since the early twentieth century. And judging by the millions of dollars in the sale of products containing probiotics, American consumers have embraced the idea despite minimal manufacturer evidence that probiotics work. Only recently have scientists begun testing probiotics in controlled, clinical trials.

In December 2007, the National Institute of Diabetes and Digestive and Kidney Diseases at the National Institutes of Health (NIH) co-sponsored the Gastrointestinal Microbiota and Advances in Prebiotic and Probiotic Research meeting to discuss the state of the science around microbial gut ecology, host-microbe interactions, and pre- and probiotics. Other sponsors included the NIH Division of Nutrition Research Coordination, the National Institute of Allergy and Infectious Diseases, the National Cancer Institute, the National Center for Complementary and Alternative Medicine, and the Office of Dietary Supplements.

Some evidence supports the use of probiotics to treat some digestive diseases, including certain types of diarrhea, a form of inflammatory bowel disease called pouchitis, and necrotizing enterocolitis in preterm infants. Most scientists at the meeting want to see more clinical trials of probiotics. Tools and data from the Human Microbiome Project will go a long way toward a better understanding of probiotics. ■

Hepatitis C Treatment Reduces Virus, Fails to Slow Progression of Disease

Long-term peginterferon therapy did not slow or prevent the progression of advanced liver disease in people with chronic hepatitis C who failed to respond to previous standard treatment, according to results of a National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) clinical trial. However, trial participants did experience significant decreases in liver enzymes, viral levels, and liver inflammation.

“The HALT-C [Hepatitis C Antiviral Long-term Treatment against Cirrhosis] Trial unequivocally demonstrated that maintenance therapy with peginterferon does not prevent progression of liver disease among patients who have failed prior treatments,” said James Everhart, M.D., a project scientist for HALT-C and a program director in the NIDDK’s

Division of Digestive Diseases and Nutrition. “These results add to the incentive to develop more effective drugs that will benefit patients with severe liver disease due to hepatitis C.”

HALT-C, a randomized, multicenter trial of 1,050 participants with chronic hepatitis C who failed prior treatment, assessed whether long-term treatment with peginterferon alfa-2a reduced the development of cirrhosis, liver failure, or liver cancer. The 517 participants randomized to the treatment arm of the study received 90 micrograms of the drug through weekly injections for 3.5 years.

The 533 participants in the control arm underwent the same follow-up and care as the treated patients, including liver biopsies, quarterly clinic visits, and blood tests. All participants had advanced liver fibrosis, a gradual scarring of the liver that puts patients at risk for progressive liver disease.

Viral hepatitis C infects more than 100 million people worldwide and as many as 4 million people within the United States.



Outcomes

Outcomes assessed in the trial were death, liver cancer, ascites—excess fluid in the abdomen—or encephalopathy, and for those who did not have cirrhosis initially, the development of cirrhosis.

At the end of the study, 34.1 percent of participants in the treated group and 33.8 percent in the control group had experienced at least one outcome. Participants in the treated group had significantly lower blood levels of the hepatitis C virus and less liver inflammation. However, there was no major difference in the rates of any primary outcomes between groups.

Among treated patients, 17 percent stopped taking peginterferon within a year and a half, and 30 percent stopped taking the drug 2 years later. Adverse events, such as infections and musculoskeletal or digestive problems, were the most common reasons people stopped taking the drug.

Viral hepatitis C infects more than 100 million people worldwide and as many as 4 million people within the United States. The virus is the most common cause of liver failure and liver cancer in the United States. The best current antiviral therapy consists of injections of pegylated interferon combined with oral ribavirin prescribed for up to 1 year. This therapy eliminates the virus in about half of infected patients.

For more information about liver disease, visit the National Digestive Diseases Information Clearinghouse at www.digestive.niddk.nih.gov. ■

Study to Explore Brain-Gut Interaction in Functional Dyspepsia Patients



Participants, whose symptoms must not be caused by depression or organic disease, will receive amitriptyline, escitalopram, or a placebo.

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) is funding a clinical study to explore the brain-gut interaction in people with functional dyspepsia and whether either of two U.S. Food and Drug Administration-approved drugs are better than a placebo in relieving the disorder's symptoms. Functional dyspepsia is a chronic condition that can cause severe stomach pain—often reported as cramping, bloating, and gas—or great discomfort or fullness after eating.

The Functional Dyspepsia Treatment Trial (FDTT) also will determine whether certain genes can predict who best will respond to treatment and whether study participants continue to respond to treatment for 6 months after they stop taking it.

During the next 5 years, researchers will enroll 400 men and women between the ages of 18 and 75 with functional dyspepsia who have failed

to respond to treatments to reduce stomach acid. Participants, whose symptoms must not be caused by depression or organic disease, will receive amitriptyline, escitalopram, or a placebo.

For information about participating in the trial, contact Vickie Silvernail, the central study coordinator, at 507-284-2812 or dyspepsia@mayo.edu. ■

NCDD Nears Finish Line on Digestive Diseases Research Agenda

The National Commission on Digestive Diseases (NCDD) has posted recommendations for public comment for a 10-year national research agenda for digestive diseases.

Commission members will reconvene this summer to approve a final report, which will be submitted to Congress and National Institutes of Health (NIH) Director Elias A. Zerhouni, M.D.

The public has 30 days to comment on the long-term research plan, available at www2.niddk.nih.gov/AboutNIDDK/CommitteesAndWorkingGroups/NCDD, which has been in development since June 2006. Slide presentations on the recommendations from the November NCDD meeting—the last time panel members convened—are also available on the website.

Commission members will reconvene this summer to approve a final report, which will be submitted to Congress and National Institutes of

Health (NIH) Director Elias A. Zerhouni, M.D. A web version of the full report with extended appendices will be available on the NCDD website.

The comprehensive research plan includes 12 chapters covering a wide range of digestive diseases and an overview of the digestive system. The congressionally mandated plan will guide the NIH, along with the investigative and lay communities, in pursuing important long-term research goals for combating digestive diseases. ■

NIH Conference Explores Problem of Fecal and Urinary Incontinence

More than a quarter of Americans will experience fecal or urinary incontinence at some point in their lives, but less than half will voluntarily report their symptoms to a health care provider, according to an independent panel appointed by the National Institutes of Health (NIH) to study the conditions.



Fecal or urinary incontinence—the inability to control bowel movements or urination—disproportionately affects women, although both men and women at all stages of life could experience the problem.

Secrecy, distress, and embarrassment related to incontinence erode the quality of life for millions of people and hamper scientific understanding and development of prevention and treatment strategies, according to the 15-member conference panel, which included experts in geriatrics, nursing, gastroenterology, obstetrics and gynecology, internal medicine, urology, general surgery, oncology, neurosurgery, and other areas of health care.

Following 3 days of meetings, the panel produced a state-of-the-science conference statement reflecting current scientific knowledge of fecal and urinary incontinence and identifying areas for further research. The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and the NIH Office of Medical Applications of Research, along with other NIH components, sponsored the conference.

Prevalence of Incontinence

Fecal or urinary incontinence—the inability to control bowel movements or urination—disproportionately affects women, although both men and women at all stages of life could experience the problem. Because routine episiotomy is associated with a higher rate of fecal incontinence, the panel recommended against the routine performance of this procedure during childbirth.

The prevalence of fecal incontinence in women increases with age, from 6 percent among those younger than 40 to 15 percent among older women, according to the panel. Between 6 and 10 percent of men experience fecal incontinence, with slight increases in prevalence as men age. The overall prevalence of fecal incontinence among nursing home residents is an estimated 45 percent.

Removing the stigma associated with incontinence would help more people with the condition get the help they need, according to the panel. Panel members recommended that health care providers address four issues when raising the subject of incontinence with their patients: frequency, volume, the degree to which symptoms are bothersome, and the desire for treatment.

The panel acknowledged that behavioral and lifestyle changes—such as getting adequate exercise, losing and maintaining weight, and not smoking—can reduce the risk of both fecal and urinary incontinence. Pelvic floor muscle training and biofeedback are effective in preventing and reversing some pregnancy-related fecal and urinary incontinence for the first year following delivery, according to the panel.

However, research about the sustained long-term benefits of pelvic floor muscle training or biofeedback in preventing fecal or urinary incontinence is insufficient. Panel members called for other interventions that increase muscle strength and mobility and standardized protocols for pelvic floor muscle training.

Additional Recommendations

Some of the panel's other recommendations addressed the need for

- uniform definitions for fecal and urinary incontinence
- more studies to estimate the direct and indirect economic and societal costs of incontinence and the potential benefits of successful prevention and treatment

NIDDK Director Honored by Hematology Society

Griffin P. Rodgers, M.D., M.A.C.P., director of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), was honored with the American Society of Hematology's Outstanding Service Award in December.



The award recognizes Rodgers' significant contributions to hematology, particularly in the areas of genetic diseases, molecular genetics of human blood cells, and human blood cell development, according to the Society. Rodgers also was honored for his efforts to increase the number of minority scholars in hematology and for becoming the first hematologist to direct the NIDDK.

"Griff Rodgers is an outstanding physician-scientist and molecular hematologist," said

National Institutes of Health Director Elias A. Zerhouni, M.D. "He's internationally recognized for contributions to the development of effective therapy for sickle cell anemia and other genetic diseases of hemoglobin, and he is also an accomplished scientific leader and mentor."

Rodgers took the helm at the NIDDK on April 1, 2007. The Institute was established in 1950. ■

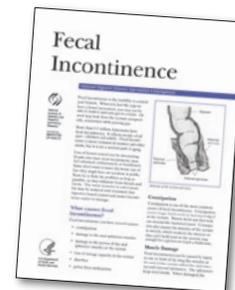
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Following 3 days of meetings, the panel produced a state-of-the-science conference statement reflecting current scientific knowledge of fecal and urinary incontinence and identifying areas for further research.

- studies to test specific hypotheses derived from the conceptual model of the causes of abnormal bowel or bladder function that could lead to incontinence
- natural history studies to identify factors affecting the incidence, progression, and remission of incontinence
- research on medical and surgical treatments that might secondarily cause incontinence, such as anorectal surgery, prostatectomy, pelvic radiation, and commonly prescribed drugs
- research to examine the impact of public health initiatives, increased public and provider awareness, reimbursement changes, and health delivery redesign

The panel's complete state-of-the-science document, which is not a policy statement of the NIH or the Federal Government, is available at www.consensus.nih.gov. Background information about the NIH Consensus Development Program Process, which includes state-of-the-science conferences, is available at www.consensus.nih.gov/forthemedial.htm.

The National Digestive Diseases Information Clearinghouse has a fact sheet about fecal incontinence at www.digestive.niddk.nih.gov/ddiseases/pubs/fecal/incontinence. ■

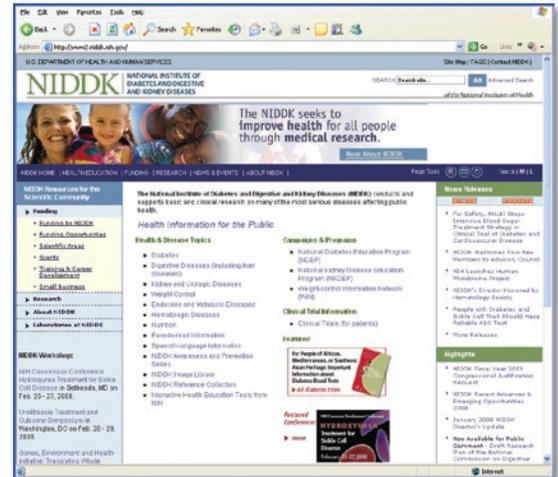


NIDDK Website Recognized as Top Performer

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) website ranked among the top five Government sites in the American Customer Satisfaction Index (ACSI) E-Government Satisfaction Index.

The ACSI E-Government Satisfaction Index is a special quarterly report of the ACSI produced by the University of Michigan in partnership with the American Society for Quality, ForeSee Results, and the CFI Group. The ACSI is a cross-industry measure of offline customer satisfaction that measures the performance of about 200 private sector companies and many Government agencies.

With a score of 85, the NIDDK was one of the top-performing sites during the last quarter of 2007. To calculate the ACSI E-Government quarterly aggregate citizen satisfaction score, ForeSee Results collects and analyzes data for more than 100 Government websites. A random sampling of site users on each of these ForeSee Results' client sites is presented with an online survey. Visitors rate the site on various components of the web experience and overall satisfaction with the website.



The high satisfaction score indicates that website users are likely to return to the site, recommend the site to other users, and use the site as a primary resource. The number-one site, with a score of 88, was the Social Security Administration's Internet Social Security Benefits Application site. ■

Upcoming Meetings, Workshops, and Conferences

Genes, Environment, and Health Initiative: Translating Whole Genome Association Data into Clinical Practice

This meeting will explore the challenges in using basic findings from the National Institutes of Health (NIH) Genes, Environment, and Health Initiative to positively affect health. The Initiative was launched in 2006 to help identify major genetic susceptibility factors for diseases with substantial public health impact and to develop technologies for measuring potentially causative environmental exposures.

The meeting, scheduled for March 10 to 11, 2008, at the NIH in Bethesda, MD, will feature presentations about important new genetic findings for inflammatory bowel disease and other illnesses, approaches to using those findings for therapeutic or diagnostic purposes, and ethical and social issues inherent in such research.

For more information and to register, visit www3.niddk.nih.gov/fund/other/GeiTranslation. ■



With a score of 85, the NIDDK was one of the top-performing sites during the last quarter of 2007.

Featured in the NIDDK Reference Collection

Liver Health

Using a liver-shaped cartoon character, this health education brochure entitled *Fifty Ways to Love Your Liver* provides basic information about the liver, its role in general health, and how readers can prevent liver damage. The brochure, which is illustrated with brightly colored graphics, also lists 50 specific strategies for how to maintain a healthy liver. The publication is available from the American Liver Foundation Information and Distribution Center, 1425 Pompton Avenue, Suite 3, Cedar Grove, NJ 07009-1000, 1-800-GO-LIVER (465-4837), ext. 234, 1-888-4 HEP-ABC (443-7222), 973-256-3214 (fax), webmail@liverfoundation.org. The cost is \$0.50 for a single copy; bulk orders are available for the cost of shipping and handling.

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) Reference Collection is a free, online database that helps health care professionals, health educators, patients, and the general public find educational materials not typically referenced in most databases. The NIDDK does not control or endorse the information contained in this collection; the information is provided as a convenience to visitors. To find more digestive diseases resources, visit www.catalog.niddk.nih.gov/resources.

Additional Resources

Awareness and Prevention Series

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) has created a new health information series to raise awareness about digestive diseases, diabetes, and kidney and urologic diseases among people not yet diagnosed with these illnesses.

The Awareness and Prevention Series, which the NIDDK developed for health fairs and similar venues, features two-page fact sheets about a wide range of health topics. Each fact sheet gives readers a snapshot of an illness, highlighting risk factors, symptoms, prevention tips, and where to go for more information. The fact sheets are written in English on one side and Spanish on the other. Digestive diseases fact sheets address foodborne illness, celiac disease, colon polyps, hepatitis, irritable bowel syndrome, and lactose intolerance.

“The series is designed to encourage readers to ask ‘Could this be me or someone I care for?’” said Kathy Kranzfelder, director of the NIDDK Information Clearinghouses. “Raising awareness of these illnesses will hopefully help people learn to prevent them or see a doctor if they have symptoms.”

Copyright-free Awareness and Prevention Series publications can be downloaded or ordered through the National Digestive Diseases Information Clearinghouse website at www.digestive.niddk.nih.gov/ddiseases/ap.htm. The website also has fact sheets and booklets with more complete information about these topics and many others related to digestive diseases.

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The Awareness and Prevention Series fact sheets are written in English on one side and Spanish on the other.

ADDITIONAL RESOURCES, from page 9



Celiac Disease

The easy-to-read booklet that explains what celiac disease is and outlines its symptoms, diagnosis, and treatment is now available in Spanish. The Celiac Disease Awareness Campaign publication *Lo que usted debe saber sobre la enfermedad celiaca* (*What you need to know about Celiac Disease*) includes an updated chart from the American Dietetic Association that lists which foods to avoid and which ones are safe to eat on a gluten-free diet.

Celiac disease is the inability to digest gluten, a protein found in wheat, rye, and barley. An estimated one in every 133 Americans suffers from celiac disease, though many have never been diagnosed and are not receiving treatment. To download a copy of the 20-page publication, go to www.digestive.niddk.nih.gov/spanish/index.asp.

Updated Fact Sheets

The National Digestive Diseases Information Clearinghouse has updated the following publications:

- *Autoimmune Hepatitis*
- *Gas in the Digestive Tract*
- *Rapid Gastric Emptying*
- *Viral Hepatitis: A through E and Beyond*
- *What I need to know about Gas*
- *Your Digestive System and How It Works*

These publications are available at www.digestive.niddk.nih.gov/ddiseases/a-z.asp.

Necrotizing Enterocolitis

“New therapies and preventive approaches for necrotizing enterocolitis (NEC): report of a research planning workshop” was published in the October 2007 issue of *Pediatric Research*. The workshop was held in July 2006 by the Digestive Diseases Interagency Coordinating Committee of the National Institute of Diabetes and Digestive and Kidney Diseases and the National Institute of Child Health and Human Development.

NEC is the death of intestinal tissue, a condition that primarily affects premature infants or sick newborns. Workshop participants agreed that finding ways to prevent NEC would be more rewarding than trying to treat the condition. ■

Correction: In the Fall 2007 issue of *Digestive Diseases News*, the sentence in the story “NIH Launches Study to Assess Bariatric Surgery in Teens” that reads “The 200 teens who will be enrolled in Teen-LABS will also be participants in adult LABS” should read as follows: “The 200 teens who will be enrolled in Teen-LABS will not be participants in adult LABS.” Two hundred adults who have consented to be part of adult LABS and have a history of obesity since their teenage years will be enrolled in Teen-LABS as a comparison group. ■